The Rejection of Claims 23-34 Under 35 U.S.C. § 112, first paragraph

Claims 23-34 are rejected as the specification allegedlly fails to demonstrate that the applicant was in possession of the claimed invention. This rejection is respectfully traversed.

It is respectfully submitted that the Patent and Trademark Office has failed to meet its burden in setting forth a *prima facie* case. The rejection asserts that it is highly unpredictable whether cancers other than those demonstrated in the working examples would be detectable by analyzing body fluids because it is unpredictable that the body fluids would contain cancer cells. See Office Action at page 3, lines 15-17. The Patent and Trademark Office fails, however, to support its assertion of unpredictability, except for noting the specification's lack of evidence. An applicant, however, need not provide a working example of every embodiment. Lack of a working example, in and of itself, does not demonstrate unpredictability. It is the Patent and Trademark Office's burden to support a rejection for non-enablement with sound scientific evidence or reasoning. Neither has been provided here.

The Patent and Trademark Office points to Table 1 of the specification as demonstrating a 60-100% non-correlation for single loci with various types of cancer. See Office Action at page 4, lines 1-10. The claims, however, require testing "a plurality of microsatellite markers" not single loci. The invention does not rely on a correlation between any particular mutant alleles and cancer. The invention uses microsatellite alterations as a passive indicator of cancer. Thus, the alleles tested need not be cancer-causing or themselves "associated with" cancer. Their alteration may merely reflect changes in DNA metabolism which occur in cancer cells. Thus, Table 1 does not provide support for the assertion of unpredictability for detecting other types of cancers in body fluids.

The Office Action asserts that if no alteration in marker length is found, then the skilled artisan would not be able to detect a cancer. (Page 9, lines 6-10) This is true, however, it says nothing more than that the artisan may obtain some false positive results. No diagnostic assay is

perfect, nor does the law require that they be. Thus, the possibility of false positive results does not indicate non-enablement.

The Patent and Trademark Office misapplies the legal formulation requiring that the applicant be in possession of the invention as of the filing date. This does not mean, that an applicant must be in possession of data demonstrating all embodiments. Similarly, the Patent and Trademark Office misapplies the legal requirement of supplying sufficient guidance and equates it to supplying working examples. One needs neither data nor working examples to fulfill 35 U.S.C. § 112, first paragraph.

Applicant was in possession of and described the full generic invention in his application when filed. Applicant provided working examples for some species. Applicant disclosed many more species. See page 8, lines 23 to page 9, line 9 (specimens). See page 11, lines 14-26 (cancers). The Patent and Trademark Office has pointed to no valid support for its bare assertion of unpredictability, nor has it articulated any type of guidance which is allegedly missing from the specification and necessary for practice. Thus, the rejection must be withdrawn for failure to make a *prima facie* case.

Applicant notes that the rejection focuses on the invention of claims 23-33, without providing separate reasoning for claim 34. Claim 34 is distinct from the other claims because it does not assess alterations in a draining biological fluid but rather in a histopathological margin. No evidence or reasoning were supplied by the Patent and Trademark Office to challenge applicant's presumptively enabling disclosure of this method. Thus, the rejection of this claim should be withdrawn.

Claims 23, 31, 35 and 36 as amended are limited to particular organs and particular draining fluids or specimens. These claims are not subject to the alleged infirmities of the generic claims.

Withdrawal of this rejection is respectfully traversed.

The Rejection of Claims 23-34 for Double Patenting

Claims 23-34 are provisionally rejected for judicially created, obviousness-type double patenting over claims 1-4, 6-9, 12-18, and 20-25 of Serial No. 08/968,733 (now allowed). The Patent and Trademark Office alleges that the instant claims include methods of detecting an allelic imbalance. It is respectfully submitted that the claims of the two applications are mutually exclusive, and that neither set of claims includes or encompasses the other.

The subject claims clearly recite determining a "microsatellite marker length alteration." The '733 claims recite comparing levels of two alleles of a heterozygous locus of an individual to determine allelic imbalance. Thus one method assesses size of a marker (length), and the other measures amount of alleles (levels). A correlate of this difference is that in the '733 method two alleles within a test sample are compared to each other, whereas in the subject method a sample marker is compared to a control marker. These are not overlapping sets of subject matter. Neither method is obvious over the other. The rejection should therefore be withdrawn.

The Rejection of Claims 23-34 for Double Patenting

Claims 23-34 are provisionally rejected over claims 1, 2, 4, 6, 8, 17, 18, 22-25, 28, 29, 31 and 35 of S.N. 09/038,637. Applicants will consider filing a terminal disclaimer of the trailing patent term of the subject application when claims in the subject application are indicated as allowable.

Respectfully submitted,

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Dated: 14 May 2001

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MARKED-UP VERSION OF AMENDMENTS MADE

IN THE CLAIMS:

23. (Amended) A method for detecting lung cancer [of an organ] in a sputum specimen [of a body fluid which drains the organ], comprising the step of:

testing a plurality of microsatellite markers in the specimen to determine a microsatellite marker length alteration relative to a control sample, wherein a microsatellite marker length alteration in the specimen relative to the control sample indicates the presence of a cancer in the lung [organ] which drains into the [body fluid] sputum.

24. (Amended) [The method of claim 23] A method for detecting cancer of an organ in a specimen of a body fluid which drains the organ, wherein the specimen is selected from the group consisting of: blood, urine, sputum, bile, stool, cervical smears, saliva, tears, cerebral spinal fluid, and lymph nodes, comprising the step of:

testing a plurality of microsatellite markers in the specimen to determine a microsatellite marker length alteration relative to a control sample, wherein a microsatellite marker length alteration in the specimen relative to the control sample indicates the presence of a cancer in the organ which drains into the body fluid.

25. (Amended) The method of claim 23, 24, or 31 wherein the length alteration is an expansion of repeat units within the microsatellite marker.

26. (Amended) The method of claim 23, 24, or 31 wherein the length alteration is a deletion of repeat units within the microsatellite marker.

27. (Amended) The method of claim 23, 24, or 31 wherein the microsatellite marker comprises a tetranucleotide repeat.

28. (Amended)The method of claim 23, 24, or 31 wherein the microsatellite marker comprises a trinucleotide repeat.

29. (Amended) The method of claim 23 wherein the [organ is head or neck] lung cancer is Small Cell Lung Carcinoma.

30. (Amended) The method of claim 23 wherein the [organ is] lung cancer is Non-Small Cell Lung Carcinoma.

31. (Amended) [The method of claim 23] A method for detecting [wherein the organ is] bladder cancer in a urine specimen, comprising the step of:

testing a plurality of microsatellite markers in the urine specimen to determine a microsatellite marker length alteration relative to a control sample, wherein a microsatellite marker length alteration in the urine specimen relative to the control sample indicates the presence of a cancer in an organ which drains into the urine.

32. The method of claim [23] 31 wherein the [specimen] cancer is [urine] Transitional Cell Carcinoma.

[33. The method of claim 23 wherein the specimen is sputum.]

34. A method for detecting cancer cells in a specimen external to a primary tumor comprising the steps of:

testing a plurality of microsatellite markers in a histopathological margin specimen external to a primary tumor to determine a microsatellite marker length alteration relative to a control sample, wherein a length alteration indicates the presence of cancer cells in the specimen.

38. (New) The method of claim 34 wherein the primary tumor is Head and Neck cancer.

39. (New) The method of claim 35 wherein the primary tumor is Squamous Cell Carcinoma.

40. (New) The method of claim 23, 24, or 31 further comprising the step of:
identifying the specimen as containing cancer cells.